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ORIGINAL CONTRIBUTION

Effect of Sesame Oil on Diuretics or ß-blockers in the Modulation of Blood Pressure, Anthropometry, Lipid Profile, and Redox Status

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The study was undertaken to investigate the effect of sesame oil in hypertensive patients who were on antihypertensive therapy either with diuretics (hydrochlorothiazide) or ß-blockers (atenolol). Thirty-two male and 18 female patients aged 35 to 60 years old were supplied sesame oil (Idhayam gingelly oil) and instructed to use it as the only edible oil for 45 days. Blood pressure, anthropometry, lipid profile, lipid peroxidation, and enzymic and non-enzymic antioxidants were measured at baseline and after 45 days of sesame oil substitution. Substitution of sesame oil brought down systolic and diastolic blood pressure to normal. The same patients were asked to withdraw sesame oil consumption for another 45 days, and the measurements were repeated at the end of withdrawal period. Withdrawal of sesame oil substitution brought back the initial blood pressure values. A significant reduction was noted in body weight and body mass index (BMI)[†] upon sesame oil substitution. No significant alterations were observed in lipid profile except triglycerides. Plasma levels of sodium reduced while potassium elevated upon the substitution of sesame oil. Lipid peroxidation (thiobarbituric acid reactive substances [TBARS]) decreased while the activities of superoxide dismutase (SOD), catalase (CAT) and the levels of vitamin C, vitamin E, ß-carotene and reduced glutathione (GSH) were increased. The results suggested that sesame oil as edible oil lowered blood pressure, decreased lipid peroxidation, and increased antioxidant status in hypertensive patients.

INTRODUCTION

Recently, much attention has been focused on the antioxidant defense system in oxidative stress and cardiovascular diseases. Natural antioxidants and polyunsaturated fatty acids contained in dietary sources are candidates for the prevention of oxidative damage and cardiovascular dis-

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[†]Abbreviations: BMI, body mass index; CAT, catalase; GPx, glutathione peroxidase; GSH, glutathione; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; PUFA, polyunsaturated fatty acids; SOD, superoxide dismutase; TBARS, thio-barbituric acid reactive substances; TC, total cholesterol.

eases [1]. Polyunsaturated fatty acids are essential for normal growth and development and may play an important role in the prevention and treatment of coronary heart disease, hypertension, diabetes, and arthritis and other inflammatory and autoimmune disorders. Clinical and epidemiological studies have shown the cardiovascular protective effects of oils rich in polyunsaturated fatty acids (PUFA) [2,3]. In particular, these substances have been reported to lower blood pressure and prevent the development of hypertension [4,5].

Sesame seeds and oil have long been categorized as traditional health food in India and other East Asian countries. Sesame oil has been found to contain considerable amounts of the sesame lignans: sesamin, episesamin, and sesamolin. Sesame oil also contains vitamin E (40 mg/100 g oil), 43 percent of polyunsaturated fatty acids, and 40 percent monounsaturated fatty acids. The lignans present in sesame oil are thought to be responsible for many of its unique chemical and physiological properties, including its antioxidant and antihypertensive properties [6-9]. In the present study, we evaluated the effect of sesame oil (rich in antioxidant lignans, vitamin E, and unsaturated fatty acids) in hypertensive patients on medication with either hydrochlorothiazide or atenolol as antihypertensive therapy.

MATERIALS AND METHODS

Subjects

The present study consists of patients of both sexes in the age group 35 to 60 years with mild to moderate hypertension, medicated with diuretics (hydrochlorothiazide) or ß-blockers (atenolol), who were recruited from the Department of Medicine at Rajah Muthiah Medical College and Hospital, Annamalai University and Prof. Maniarasan Memorial Polyclinic, Chidambaram, Tamilnadu, India. The criterion for hypertension was systolic blood pressure greater than or equal to 140 mm Hg and diastolic blood pressure greater than or equal to 90 mm Hg, recorded on at least three different occasions after they had rested for 10 minutes supine. Patients with secondary hypertension, hypertension associated with diabetes mellitus, chronic alcoholism, female patients on oral contraceptives, pregnant females, and lactating mothers were excluded from the study. All the subjects gave informed consent to undergo the investigations, and the Ethical committee of Rajah Muthiah Medical College, Annamalai University, Tamilnadu, India, approved the study.

Study design

A detailed clinical history and physical examination were performed at baseline, and the following measurements were taken: blood pressure; anthropometric measurements such as height, weight, and body mass index (BMI); lipid profile (total cholesterol [TC], high density lipoprotein cholesterol [HDL-C], low density lipoprotein cholesterol [LDL-C], and triglycerides [TG]); electrolytes (Na^+, K^+); lipid peroxidation (TBARS); and enzymic and non-enzymic antioxidants in blood. The patients were advised to continue their antihypertensive drugs as usual. The patients were on medication with hydrochlorothiazide or atenolol for one year prior to the enrollment in the study. The patients were supplied 4 to 5 kg of sesame oil (Idhayam gingelly oil) for a four-member family per month, which constitutes approximately 35 g of oil/day/person. The patients were asked to use sesame oil as the only edible oil for 45 days. At the end of the 45th day, the investigations were repeated. Finally, the patients were asked to switch over to whatever original oil they had been taking before the enrollment of the study for another 45 days. Mostly they were using either sesame oil, groundnut oil, or palm oil interchangeably. All the measurements were repeated at the end of the 90th day of our experiment. The patients were told to strictly adhere to the study protocol. Those who could not follow the protocol until the end of the experiment for any reason were excluded. To avoid much difference in dietary patterns and caloric changes, the same patients have been subjected to

Table 1. Blood pressure and anthropometric measurements at baseline, sesame oil substitution, and withdrawal of sesame oil (values represent means ± SD).

	Age 35 to 60 (n = 50)		
Parameters	**Baseline**	**Sesame oil substitution**	**Withdrawal of sesame oil**
Systolic blood pressure (mm Hg)	144.25 ± 10.50	124.88 ± 8.0[a]	144.85 ± 10.50[1]
Diastolic blood pressure (mm Hg)	97.9 ± 7.80	83.80 ± 6.0[a]	97.60 ± 7.56[1]
Height (cm)		159.9 ± 5.0	
Weight (kg)	74.30 ± 7.5	68.5 ± 7.0[a]	70.0 ± 7.0[b]
Body mass index	29.40 ± 3.0	27.08 ± 3.30[a]	27.7 ± 1.90[a]

a,1 $p < 0.001$; b $p < 0.01$
a, b – as compared with baseline value
1 – as compared with sesame oil substitution

substitution of sesame oil and withdrawal of sesame oil substitution.

Anthropometric and blood pressure measurements

Body weight was measured, using a level balance, to the nearest 0.1 kg. Body height was measured without footwear to the nearest 0.5 cm. BMI was calculated as weight (in kg)/height (in m^2). Blood pressure was measured by using standard mercury sphygmomanometer

Biochemical analysis

Fasting blood samples were collected on entering the study (0 days), at the end of 45 days, and after 90 days (i.e., after substitution and withdrawal). Lipid profile, electrolytes, lipid peroxidation, and enzymatic and non-enzymic antioxidants were estimated at the three experimental periods: baseline, after sesame oil substitution, and after withdrawal of sesame oil. All the biochemical determinations were carried out in the Biochemistry Laboratories at Department of Biochemistry, Faculty of Science or Rajah Muthiah Medical College and Hospital, Annamalai University. TC [10], HDL-C [11], and TG [12] concentrations in plasma were determined by standard enzymic methods with a semiautoanalyser (Bayer RA 150, Germany) using commercially available kits (Biocon, Germany). LDL-C was calculated using Friedwald equation [13]. Sodium and potassium [14], TBARS [15], enzymic antioxidants such as superoxide dismutase (SOD) [16], catalase (CAT) [17], glutathione peroxidase (GPx) [18], and non-enzymic antioxidants such as vitamin C [19], vitamin E [20], ß-carotene [21], and reduced glutathione (GSH) [22] also were estimated.

Statistics

Student's t test was applied for comparison between two related samples; values for continuous variables are expressed as means ± SD.

RESULTS

Table 1 shows blood pressure and anthropometric measurements at baseline, sesame oil substitution, and withdrawal of sesame oil. Replacement of sesame oil as cooking oil in hypertensive patients brought their systolic and diastolic blood pressure to normal in a statistically significant fashion. Significant reduction in body weight and body mass index also was noted. After the withdrawal of sesame oil substitution, the values rose again.

Table 2 shows the plasma lipid profile at baseline, after sesame oil substitution, and after withdrawal of sesame oil. No significant alterations were seen in TC, HDL-C, LDL-C, and the TC/HDL-C ratio. TG levels decreased significantly and then rose, following sesame oil substitution and withdrawal, respectively.

Table 3 shows the plasma levels of electrolytes at baseline, after sesame oil substi-

Table 2. Lipid profile at baseline, sesame oil substitution, and withdrawal of sesame oil (values represent means ± SD).

	Age 35 to 60 (n = 50)		
Parameters	**Baseline**	**Sesame oil substitution**	**Withdrawal of sesame oil**
TC (mg/dl)	220 ± 15.5	217 ± 18.0	223 ± 20.0
HDL-C (mg/dl)	46.0 ± 2.5	47.0 ± 1.8	46.5 ± 2.4
LDL-C (mg/dl)	136.0 ± 7.0	138.0 ± 11.0	139.0 ± 16.4
TG (mg/dl)	194.80 ± 8.5	159 ± 9.0[a]	179.9 ± 11.50[a,1]
TC/HDL ratio	4.8 ± 1.7	4.7 ± 1.0	4.76 ± 1.5

a,1 $p < 0.001$
a – as compared with baseline value
1– as compared with sesame oil substitution

tution, and after withdrawal of sesame oil. Plasma sodium levels decreased significantly and then rose, following sesame oil substitution and withdrawal, respectively. Potassium levels increased significantly upon sesame oil substitution and subsequently decreased, but within normal limits.

Table 4 shows the levels of TBARS, enzymic and non-enzymic antioxidants at baseline, after sesame oil substitution, and after withdrawal of sesame oil. Significant reduction in TBARS was noted, and the values were almost maintained even after withdrawal of sesame oil. Plasma CAT and erythrocyte membrane bound SOD activities significantly increased, while erythrocyte membrane bound GPx activity decreased gradually from sesame oil substitution to withdrawal. Significant elevations of vitamin C, vitamin E, ß-carotene, and reduced glutathione were observed, and the levels decreased once sesame oil substitution was stopped.

DISCUSSION

In the present study, substitution of sesame oil lowered systolic and diastolic blood pressure remarkably in hypertensive patients. Studies reported that sesamin, a lignan from sesame oil, exerts antihypertensive action by interfering with renin-angiotensin system, as the lignan is more effective on the renin-independent DOCA (Deoxycorticosterone acetate) -salt hypertension than on the renin-independent 2K (two kidney), 1C (one clip) renal hypertensive model [6, 8]. In another study using the rat aortic ring, sesamin produced Ca^{2+} antagonistic vasodilatory activity [8]. This pharmacological action, at least in part, may contribute to its antihypertensive activity. Natural antioxidants and polyunsaturated fatty acids show protective function against hypertension [1]. Supplementation of vitamin E reduced blood pressure in mild hypertensive patients and was associated with a remarkable decrease in

Table 3. Electrolytes at baseline, sesame oil substitution, and withdrawal of sesame oil (values represent means ± SD).

	Age 35 to 60 (n = 50)		
Parameters	**Baseline**	**Sesame oil substitution**	**Withdrawal of sesame oil**
Sodium (mEq/l)	137.5 ± 1.5	130.0 ± 1.0[a]	136.5 ± 1.8[1]
Potassium (mEq/l)	4.0 ± 0.18	4.72 ± 1.15[a]	4.05 ± 0.18[1]

a,1 $p < 0.001$
a – as compared with baseline value
1– as compared with sesame oil substitution

Table 4. TBARS, enymic, and non-enzymic antioxidants at baseline, sesame oil substitution, and withdrawal of sesame oil.

	Age 35 to 60 (n = 50)		
Parameters	**Baseline**	**Sesame oil substitution**	**Withdrawal of sesame oil**
TBARS (nmol/dl)	6.0 ± 1.40	3.40 ± 0.80[a]	3.20 ± 0.82[a]
E SOD (U^x/mg Hb)	3.0 ± 0.46	4.70 ± 0.70[a]	3.6 ± 0.14[b,1]
E GPx (U^y/min mg Hb)	8.80 ± 0.51	7.70 ± 0.12[a]	5.40 ± 0.15[a,1]
P CAT (U^z/mg protein)	5.4 ± 0.34	7.21 ± 0.66[a]	5.67 ± 0.35[1]
Vitamin C (mg/dl)	0.90 ± 0.09	1.08 ± 0.09[a]	0.80 ± 0.10[c,1]
Vitamin E (mg/dl)	1.60 ± 0.44	2.0 ± 0.20[a]	1.40 ± 0.20[d,1]
ß-carotene (mg/dl)	0.50 ± 0.08	0.70 ± 0.05[b]	0.50 ± 0.03[2]
Reduced glutathione (mg/dl)	15.0 ± 3.0	27.5 ± 3.0[a]	18.5 ± 2.0[b,1]

a,1 $p < 0.001$; b,2 $p < 0.01$; c,3 $p < 0.05$; d,4 $p < 0.02$
a, b,c,d – as compared with baseline value
1,2,3,4 – as compared with sesame oil substitution
P, Plasma; E, Erythrocyte membrane; ^{x} One unit of activity was taken as the enzyme concentration which gave 50 percent inhibition of NBT reduction in one minute; ^{y} µg of glutathione consumed/min/mg Hb; ^{z} µmole of H_2O_2 consumed/min/mg protein.

systolic and diastolic blood pressure [23]. The fatty acid composition of dietary fat is a key determinant of membrane fatty acid composition [24]. As PUFA substitution increases the fluidity of the bilipid layers, the distensibility of biomembranes may increase. The blood pressure-lowering effect of sesame oil may be due to its richness of antioxidant lignans (sesamin, episesamin, sesamol, and sesamolin), vitamin E, and unsaturated fatty acids.

The risk of hypertension increases progressively with higher levels of body weight or BMI and parallels the degree of obesity. The association between BMI and blood pressure consistently has been shown in numerous studies [25]. Numerous studies consistently have documented that for those who are already overweight, weight loss significantly reduces blood pressure and the incidence of subsequent hypertension. Large, randomized trials of weight reduction in adults with hypertension have shown significant reductions in blood pressure in response to weight loss [26]. Studies suggest that polyunsaturated fatty acid increases the plasma levels of leptin, which, in turn, would facilitate the reductions of weight [27]. Polyunsaturated fatty acids in sesame oil also may play a role in the reduction of body weight in our study, which in turn may reduce the blood pressure. The reduction of body weight and body mass index in our study mainly may be due to sesame oil substitution, since the values increased once the sesame oil substitution was withdrawn.

Prior studies in rats have been shown that sesame lignans (sesamin and/or episesamin) lower serum and liver cholesterol concentrations by inhibiting absorption and synthesis of cholesterol [28]. We did not find a cholesterol-lowering effect in hypertensive patients on medication with diuretics or ß-blockers. This may be due to the negative effect of diuretics and ß-blockers on lipids. Recently, the Scientific Advisory of the American Heart Association reported that high monounsaturated fatty acids diets tend to lower triglyceride concentrations [29]. We found that substitution of sesame oil as edible oil lowered plasma triglyceride concentrations.

Reports suggested that antihypertensive compounds modulate the Na^+-K^+ pump and thereby maintain the electrolytes levels in hypertensive patients. Cardiac output is influenced by blood volume, which is greatly dependent on body sodium. Thus, sodium excretion is central to blood pressure modulation. Decreasing sodium excretion increases fluid volume and leads to high cardiac output. Potassium can influence cell

membrane stabilization and vascular smooth muscle relaxation [1]. In our present study, we found that plasma levels of sodium decreased while potassium levels increased upon the substitution of sesame oil. However, the mechanism of reduction of sodium and elevation of potassium upon sesame oil substitution is not known.

Thiobarbituric acid reactive substances, a measure of lipid peroxidation, decreased significantly upon sesame oil substitution. It has been reported that sesamolin, a lignan present in sesame oil, reduced lipid peroxidation in rats [30]. Sesamin and sesamolin may potentiate the effect of vitamin E and they themselves act as antioxidants, which, in turn, may reduce lipid peroxidation. In our study, plasma levels of TBARS did not change even after withdrawal of sesame oil substitution. Perhaps the lignans stored in the body may be responsible for this.

The role of the antioxidant defense system, which includes superoxide dismutase (EC 1.15.1.1; Cu/Zn SOD), catalase (EC 1.11.1.6; CAT), and glutathione peroxidase (EC 1.11.1.9; GSH-Px), in protection against oxidative insults is well characterized, and it has been suggested that this antioxidant defense system may be influenced by nutrition [31]. Enzymatic antioxidants, such as SOD and CAT, play an important role in the conversion of ROS to oxygen and water. SOD is a well-known scavenger enzyme preventing the cell from oxidative stress. CAT is an important antioxidant enzyme whose physiological role is to detoxify H_2O_2 into oxygen and water and thus limit the deleterious effects of reactive oxygen species. Cells maintain their vital functions against oxidative damage with the help of a system that involves GPx, SOD, CAT, glutathione reductase, some trace elements, and vitamins A and E. The increase of SOD and CAT may be due to decreased utilization, since lipid peroxidation levels are low. GPx decreased probably due to the decreased synthesis, since lipidperoxidation levels were low. Vitamin E has been recognized as one of the body's major natural antioxidants. Sesame oil contains 40 mg of vitamin E per 100 g of oil [32]. Vitamin E has several potentially cardio-protective effects: It decreases lipid peroxidation and spares glutathione [33, 34]. Vitamin E has been shown to lower blood pressure in spontaneously hypertensive rats [35]. In the present study, plasma levels of vitamin E increased upon substitution, which could be due to the greater availability of vitamin E in sesame oil.

Elevation of vitamin C upon the substitution of sesame oil could be due to the decreased utilization or due to increase in the levels of GSH, because vitamin C and GSH are synergistic antioxidants [36]. Epidemiological reports show that carotenoids may play a preventive role in cardiovascular disease [37]. Plasma levels of ß-carotene rose significantly upon the substitution of sesame oil, which could be due to the sparing action of vitamin E and sesame lignans.

In conclusion, substitution of sesame oil, as the sole edible oil, lowered blood pressure in hypertensive patients who were taking diuretics and ß-blockers. Sesame oil also has beneficial effects on the levels of triglyceride, electrolytes, lipid peroxidation, and antioxidants.

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